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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,300	09/24/2004	Yung-Hi Kim	OPA9408-32/US	3662

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EXAMINER	
GRAFFEO, MICHEL	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,300	KIM ET AL.	
	Examiner	Art Unit	
	Michel Graffeo	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-18,21,22 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-18,21,22 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *24 Sep 04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II claims 6-18, 21-22 and 24-25 in the reply filed on 23 January 2006 is acknowledged.

Status of Action

The Amendment filed 23 January 2006 canceled claims 1-5, 19-20 and 23 and added claims 26-29. Claims 6-18, 21-22 and 24-29 are pending and examined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 24-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The phrases "Use of" and "The use of" constitute non-statutory claim language. Further, the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

However, in order to advance prosecution these claims will be examined as method of use claims.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-18, 21-22 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting IL-8 in vitro and treating sepsis to the extent that survival rates of septicemia induced mice are better as compared to the control, does not reasonably provide enablement for the treatment and/or prevention of any and all diseases associated with IL-8, i.e. Gerhardt disease and ischemia-reperfusion injury. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation.

The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;

6) the quantity of experimentation necessary;
7) the state of the prior art; and ,
8) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1) the nature of the invention; the invention is directed to a method of treating and/or preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury.

2) the breadth of the claims; the scope of the method claims includes the treatment and prevention of any and all diseases associated with IL-8, i.e. Gerhardt disease and ischemia-reperfusion injury but has not recited the step(s) that (a) result in preventing nor treating all claimed disease nor (b) having a specified end result of the treatment.

3) the predictability or unpredictability of the art; the ability of preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury is not yet known in the art. See, Riedermann et al. Anti-inflammatory strategies for the treatment of sepsis. *Expert Opin. Biol. Ther.* (2003) 3(2):339-350 which reviews some symptoms and treatments for sepsis and ultimately concludes that the 'silver bullet' therefor has not yet been found (page 346). The burden of enabling one skilled in the art to treat and prevent any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury would be much greater than that of enabling the treatment of such diseases. In the instant case, the specification does not provide guidance as to how one skilled in the art would

accomplish the objective of preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for preventing such a list of diseases (see for example claim 17).

No experimental evidence supporting the contention that the claim specified actives could actually prevent these diseases by simply administering the claim specified active agents has not been demonstrated. The specification fails to enable one of ordinary skill in the art to practice the presently claimed method for preventing and for practicing same without a specific endpoint for the treatment of the claimed diseases.

The term "prevention" or "preventing" is synonymous with the term "curing" and both circumscribe methods of treatment having absolute success. Since absolute success is not as of yet reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations which are as complex/poorly understood as sepsis, inflammatory bowel disease, meningitis MS etc., the specification is viewed as lacking enablement for prevention for any of the diseases/conditions recited, in e.g., claim 17.

4) the amount of direction or guidance presented; the specification does not provide any guidance in terms of preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury.

5) the presence or absence of working examples; no working examples are provided for preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury, for example in a patient, in the specification. The applicant has not provided any competent evidence or disclosed any tests that are highly predictive for the preventative effects of the instant composition. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

6) the quantity of experimentation necessary; the quantity of experimentation would be an undue burden to one of ordinary skill in the art and amount to the trial and error type of experimentation. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. To support a claim to prevent or treat all claimed diseases, Applicant would need to provide confirmative in vivo data supporting an absolute prevention of the diseases as well as dosage regimes resulting in the prevention of same.

In view of the breadth of the claims, the chemical nature of the invention and unpredictability of preventing of any and all diseases associated with IL-8, i.e. sepsis and ischemia-reperfusion injury, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an

undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

In consideration of each of factors 1-6, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, applicant must convey with reasonable clarity to one skilled in the art, as of the filing date that application was in possession of the claimed invention. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Possession may be shown in many ways. For example, possession may be shown by describing an actual reduction to practice of the claimed invention. Possession may also be shown by a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention. An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. For example, a specification may describe an actual reduction to practice by showing that the inventor constructed an embodiment or performed a process that met all the limitations of the claim and determined that the invention would work for its intended purpose or an applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole.

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to

practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]."

Applicant has not conveyed possession of the invention with reasonable clarity to one skilled in the art. The scope of claim 6 has no limitations in terms of G2A receptor ligands. Applicant has not provided any working examples which would describe one of ordinary skill in the art an embodiment that met all the limitations of thereof. In other words, the Applicant has not described with sufficient clarity all G2A receptor ligands, known and unknown. The few species examples provided are not sufficient to describe, absent any evidence of working examples representative of the genus of compositions contemplated in claim 6, nor are they sufficient to provide predictable operability of the invention to one of ordinary skill in the art.

Claim Rejections - 35 USC § 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24-25 are rejected under 35 USC § 112 2nd paragraph as being indefinite even though they provide for the use of an agonist ligand specific to G2A receptor, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 6 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 and 11 are of indeterminate scope. Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since, the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. Moreover, determining whether a given disease responds or not to modulation at one or more receptor sites involves much experimentation since a negative response from one patient does not necessarily mean the drug isn't useful, as no drug has 100% effectiveness. Thus, what success rate determines if a particular inhibitor is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112,

paragraph two, is whether applicants have clearly defined their invention, not what may be discovered by feature research as this type of claim language clearly requires.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-22 and 26-29 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,746,652 to Buckalaw Jr. et al.

Buckalew Jr. et al. teach the claimed compounds in col 2 lines 5-45. In addition, please note that the recitation of an intended use, e.g., "treatment of _", does not lend patentable weight to composition claims. Therefore, a claim to a known compound is examined without regard to the compound's intended use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-18, 21-22 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rikitake et al. Expression of G2A, a Receptor for Lysophosphatidylcholine by Macrophages in Murine, Rabbit and Human Atherosclerotic Plaques. Arterioscler Thromb Vasc Biolo (2002) pg 2049-2053 in view of Falcone et al. Ascaris suum-Derived Products Induce Human Neutrophil Activation via a G Protein-Coupled Receptor that Interacts with the Interleukin-8 Receptor Pathway. Infection and Immunity (2001) Vol 69, No. 6 pp. 4007-4018 and further in view of US Patent No. 6,515,001 to Saxena et al.

Rikitake et al. teach that the G2A is a high affinity receptor for lysophosphatidylcholine (LPC) (in current claims 6-18, 21-22 and 24-25; see Abstract and introduction).

Rikitake et al. do not specifically recite the inhibition of IL-8 with LPC.

Falcone et al. teach that chemokines act on target cells through G protein coupled receptors and that the engagement of a G protein coupled receptor with an agonist results in a panoply of possible functional cellular responses (in current claims 6-18, 21-22 and 24-25; see page 4008).

Saxena et al. teach that IL-8 is involved in inflammatory conditions such as psoriasis (in current claim 17; see col 2 lines 41-43) and in the participation of inflammatory cells in atherosclerosis, a process that is thought to involve chemotactic cytokines, which may play a role in cellular entry into the vessel wall. Consistent with this, IL-8 and its receptor CXCR-2 are expressed on macrophages (Mphi) in atherosclerosis in mice (in current claims 6-18, 21-22 and 24-25; col 3 lines 45-55).

One of ordinary skill in the art would have been motivated to combine the above references and as combined teach the claimed invention as claimed. One of ordinary skill in the art would have been motivated to combine Rikitake et al. with Falcone et al. because Falcone et al. teach that by engaging the G protein coupled receptors, various cellular responses result such as functional cellular responses, most of which are rapid and transient, for example a characteristic rise in the cytosolic calcium concentration (see page 4008) and Rikitake et al. in turn teach that LPC is known to increase intracellular calcium concentration and activate the divergent intracellular signal cascades (see introduction). Saxena et al. in turn discuss IL-8 in the participation of inflammatory cells in atherosclerosis along with a general discussion of the status of knowledge in the art about IL-8, whereas Rikitake et al. teach that G2A is involved in the formation and progression of atherosclerotic lesions. Based on Rikitake et al. solely, one of ordinary skill in the art would expect that LPC to treat a number of diseases as comprehensive as the list in claim 17 whereas Falcone et al. and Saxena et al. express that which is naturally and necessarily occurring i.e. LPC effects mediated via the IL-8

receptor pathway. Thus, the combined references teach and make prima facie obvious how to use the claimed invention at the time that it was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-18, 21-22 and 24-25 are provisionally rejected on the ground of nonstatutory double patenting over claims 1, 3 and 5 of copending Application No. 10/475814. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is claimed disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant

application are claiming common subject matter, as follows: a method of treating a disease associated with inflammation, sepsis for example, with LPC and a composition comprising LPC.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

15 March 2006
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